Application for United States Letters Patent

For:

APPETITE STIMULATION AND REDUCTION OF WEIGHT LOSS IN PATIENTS SUFFERING FROM SYMPTOMATIC HIV INFECTION

By:

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BACKGROUND OF THE INVENTION

Among the many problems endured by patients suffering from symptomatic HIV infection, which includes inter alia AIDS (Acquired Immune Deficiency Syndrome) and ARC (AIDS Related Complex), are loss of appetite with consequent loss of weight. This loss of appetite and loss of weight further debilitates the patients and increases the many problems associated with the HIV infection.

The compound delta-9-tetrahydrocannabinol, which is the active ingredient in marijuana and which was produced chemically as described in Patent No. 3,668,224, has been used as an antiemetic to relieve nausea and vomiting in patients receiving cancer chemotherapy.

A number of cancer investigators have used delta-9-tetrahydrocannabinol to attempt to increase appetite and modify weight loss in cancer patients. For example, in a randomized double-blind crossover study employing oral delta-9-tetrahydrocannabinol and prochlorperazine, 50% of the subjects on delta-9-tetrahydrocannabinol reported an increased food intake while only 29% had a similar response on the prochlorperazine.[1] In another study of similar design and using the same medications, patients on delta-9-

[1] Sallan, SE; Cronin, C; Zelan, M; and Zinberg, NE (Sidney Farber Cancer Institute, Boston, Massachusetts): Antiemetics in patients receiveing chemotherapy for cancer. A prochlorperazine. N. Engl. J. Med. 301:135-138 (Jan. 17) 1980, No. 3.

tetrahydrocannabinol reported feeling more hungry than patients on prochlorperazine.[2] Results suggestive of an appetite stimulating effect were also noted by Ekert, et al.[3] in groups of children and adolescents 6-19 years of age administered delta-9-tetrahydrocannabinol, prochlorperazine or metaclopramide in crossover design studies.

In a double blind study, Regelson, et al.[4] observed that advanced cancer patients on chemotherapy receiving delta-9-tetrahydrocannabinol maintained their weight better than those not receiving the delta-9-tetrahydrocannabinol.

In an open study, Wadleigh, et al.[5] observed appetite increases and a lessening of the rate of weight loss in cancer patients.

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[2] Ungerleider, JT; Andrysiak, T; Fairbanks, L; Gooodnight, J; Sarna, G; and Jamison, K. (UCLA Center for the Health Sciences, Los Angeles, California): Cannabis and cancer chemotherapy. A comparison of oral delta-9-THC and prochlorperazine.Cancer 50:636-645 (Aug. 15) 1982, No. 4.

[3] Ekert, H; Waters, KD; Jurk, IH; Mobilia, J; and Loughnan, P. (Royal Children's Hospital, Melbourne, Australia): Amerlioration of cancer chemotherapy-induced nausea and vomiting by delta-9-tetrahydrocannabinol.Med. J. Aust. 2:657-659 (Dec. 15) 1979.

[4] Regelson W, Butter JR; Schultz J; Kirk T; Peek L; Green ML; Delta-9-tetrahydrocannabinol, (delta-9-THC) as an effective antidepressant and appetite-stimulating agent in advanced cancer patients.The pharmacology of marihuana, (Braude MC & Szara S eds) Raven Press, N.Y. (1976; pp. 763-766.

[5] Wadleigh, R; Spaulding, M; Lembersky, B; Zimmer. M: Shepard, K; Plasse, T; Dronabinol enhancement of appetite in cancer patients. Proceedings 1990 American Cancer Society of Clinical Mycology Meeting.

SUMMARY OF THE INVENTION

It is accordingly a primary object of the present invention to provide for the treatment of patients suffering from symptomatic HIV infection so as to improve the appetite and reduce weight loss in such patients.

Other objects and advantages of the present invention will be apparent from a further reading of the specification and of the appended claims.

With the above and other objects in view, the present invention mainly comprises the administration to a patient suffering from symptomatic HIV infection of an appetite stimulating effective amount of delta-9-tetrahydrocannabinol.

The delta-9-tetrahydrocannabinol is preferably administered orally as dronabinol (delta-9-tetrahydrocannabinol in sesame oil-containing capsules). Administration is also possible to achieve the effects of the present invention when the delta-9-tetrahydrocannabinol is in the form of tablets, suppositories, intranasal administration, transdermal administration, inhalants and sublingual administration, as well as administration by injection.

The dosage range of delta-9-tetrahydrocannabinol may vary widely from 2.5 mg to 20 mg daily, in single or divided doses.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The following is given to further illustrate the present invention. The scope of the invention is not,

however, meant to be limited to the specific details thereof.

EXAMPLE I

Soft gelatin capsules were filled with delta-9-tetrahydrocannabinol in sesame oil (dronabinol). Capsules were filled with 2.5 mg delta-9-tetrahydrocannabinol per capsule or 5 mg delta-9-tetrahydrocannabinol per capsule.

Ten symptomatic HIV patients were treated with delta-9-tetrahydrocannabinol. The patients studied were all homosexual males; one had a history of intravenous drug abuse as well. The infectious complications which they had represent the spectrum of those usually seen in a symptomatic HIV-infected population.

Most of the patients had received or were on antiviral therapy, primarily zidovudine (azidothymidine). Two had previously received and one was receiving megesterol acetate as well. Patients received delta-9-tetrahydrocannabinol as dronabinol (delta-9-tetrahydrocannabinol in sesame oil in soft gelatin capsules), usually at a dose of 2.5 mg, for one to five months. Treatment continued for most of the patients at the time of this analysis. The dose varied. The patients were instructed to take medication up to four times daily as needed; many took it somewhat less often.

Initially, patients were losing a median of 0.93 kg/mo. On therapy, they gained 0.54 kg/mo. The median difference on versus pre-therapy was 1.92 kg/mo. Seven patients gained

weight while two others had a decrease in weight loss. This result was unexpected as previous studies in cancer patients showed that while weight loss lessened, patients rarely gained weight.

EXAMPLE II

In a prospective, dose-ranging study, 23 patients with symptomatic HIV infection were treated with dronabinol at a dose of 2.5 mg twice daily to 5.0 mg three times daily. Of these, 13 completed approximately one month on therapy. Of those completing one month on therapy, seven gained weight.

At a dose which appears optimal, seven of eight patients completed one month treatment. At that dose, most patients did not experience side effects. Most of those patients who did experience side effects found them tolerable. Confirming the unexpected results of Example I, five of the seven patients gained weight. The median rate of weight loss prior to therapy was 1.62 kg/mo; on therapy, the median weight gain was 1.56 kg/mo. The median improvement in the rate of weight change was 3.06 kg/mo, or approximately 1.5 lbs/wk.

It thus appears that delta-9-tetrahydrocannabinol can provide a significant tool in the treatment of patients with symptomatic HIV infection by improving appetite and reducing

weight loss.

While the invention has been illustrated with respect to specific dosages, it is apparent that variations and modifications can be made without departing from the spirit or scope of the invention.